

Application No. 09/426,776

***Claims pending in this application:*****NUCLEOTIDES ENCODING SECRETORY SIGNALS**

1. (amended) An isolated nucleic acid comprising a nucleotide sequence encoding a secretory signal sequence comprising the amino acid sequence SEQ ID NO:10, or variants of said amino acid sequence that comprise conservative replacements thereof that retain the biological activities of directing secretion of a fusion protein from a cell and cleavage of the secretory signal sequence from the fusion protein.
2. (amended) The isolated nucleic acid of claim 1, wherein the nucleotide sequence encoding the secretory signal sequence is SEQ ID NO:11.
3. (amended) The isolated nucleic acid of claim 1, wherein the cell from which secretion is directed is a eukaryotic cell.
4. (amended) The isolated nucleic acid of claim 1, wherein the cell from which secretion is directed is a prokaryotic cell.
5. (amended) The isolated nucleic acid of claim 1, wherein the secretory signal sequence is cleaved between the G and D residues in the VGDQ portion thereof.
6. (amended) The isolated nucleic acid of claim 3, wherein the secretory signal sequence is cleaved between the G and D residues in the VGDQ portion thereof.

Application No. 09/426,776

26. (amended) An isolated nucleic acid comprising a nucleotide sequence encoding a fusion protein comprising a secretory signal sequence and a desired protein;

wherein said secretory signal sequence comprises the amino acid sequence SEQ ID NO:10, or variants of said amino acid sequence that comprise conservative replacements thereof that retain the biological activities of directing secretion of the fusion protein from a cell and cleavage of the secretory signal sequence from the fusion protein;

wherein the desired protein is joined to the carboxy-terminus of the secretory signal sequence, either directly or by a linking amino acid sequence.

7. (amended) The isolated nucleic acid of claim 26 wherein said desired protein is a reporter protein.

8. (amended) The isolated nucleic acid of claim 7, wherein the nucleotide sequence encoding the secretory signal sequence is SEQ ID NO:11.

9. (amended) The isolated nucleic acid of claim 7, wherein the reporter protein is selected from the group consisting of chloramphenicol aminotransferase, green fluorescent protein or another aequorin,  $\beta$ -amylase,  $\beta$ -lactamase, luciferase, glucuronidase, alkaline phosphatase, and  $\beta$ -galactosidase.

Application No. 09/426,776

11. (amended) The isolated nucleic acid of claim 26 wherein said desired protein is a lipopolysaccharide-binding protein.

12. (amended) The isolated nucleic acid of claim 11, wherein the lipopolysaccharide-binding protein is Factor C from a horseshoe crab, or a variant thereof -- comprising conserved amino acid replacements or insertions or deletions -- that retains lipopolysaccharide-binding activity.

13. (amended) The isolated nucleic acid of claim 11, wherein the nucleotide sequence encoding the secretory signal sequence is SEQ ID NO:11.

VECTORS AND HOST CELLS

15. (amended) A recombinant vector comprising the isolated nucleic acid of any one of claims 1-6.

16. (amended) A host cell transformed with the recombinant vector of claim 15.

17. (amended) The recombinant host cell of claim 16, wherein said cell is selected from the group consisting of a bacterial cell, a COS cell, a CHO cell, a NIH/3T3 cell, a Schneider 2 cell, a *S. cerevisiae* cell, and an EPC cell.

32. A recombinant vector comprising the isolated nucleic acid of claim 26.

27. (amended) A host cell transformed with the recombinant vector of claim 32.

Application No. 09/426,776

PROTEINS AND THEIR PRODUCTION

28. (amended) A method for producing a desired protein comprising culturing a host cell of claim 27 under conditions wherein the desired protein is secreted from the host cell; and

recovering the desired protein from the culture medium.

29. (amended) A fusion protein comprising

(i) a secretory signal sequence polypeptide comprising the amino acid sequence SEQ ID NO:10, or variants of said amino acid sequence that comprise conservative replacements thereof that retain the biological activities of directing secretion of a fusion protein from a cell and cleavage of the secretory signal sequence from the fusion protein, and

(ii) a second polypeptide.

30. (amended) The fusion protein of claim 29, wherein the second polypeptide is a lipopolysaccharide binding protein.

31. (amended) The fusion protein of claim 29, wherein the second polypeptide is a protein selected from the group consisting of chloramphenicol aminotransferase, green fluorescent protein or another aequorin,  $\beta$ -amylase,  $\beta$ -lactamase, luciferase, glucuronidase, alkaline phosphatase, and  $\beta$ -galactosidase.